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Introduction to the Treatment of Stimulant Use Disorders

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Territory Acknowledgement

I respectfully acknowledge the land on which I live and work is the traditional territory of the Coast Salish Peoples, including the unceded homelands of the x^wməθkwəy'əm (Musqueam), Sk̓wxwú7mesh (Squamish), and sə'ílwətał (Tsleil-Waututh) Nations.

Disclosures

- Research grants from Michael Smith Health Research BC and the Canadian Institutes of Health Research (CIHR)

*The content of this activity may include discussion of off label or investigative drug uses.
The faculty is aware that it is their responsibility to disclose this information.*

Educational Objectives

- At the conclusion of this activity participants should be able to:
 - Describe the most commonly used unregulated stimulants
 - Appreciate shifts in patterns of use and health consequences over time in North America
 - Adopt a formal approach to the assessment of stimulant use including:
 - Intoxication & withdrawal management
 - Psychosocial treatments
 - Pharmacological treatments
 - Apply a harm reduction lens to stimulant use

Background

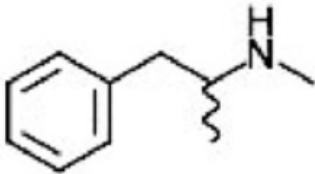
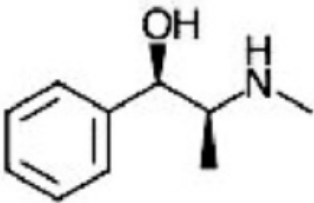
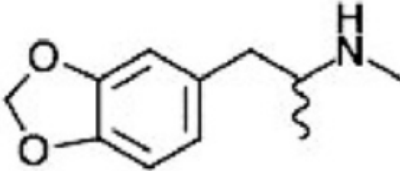
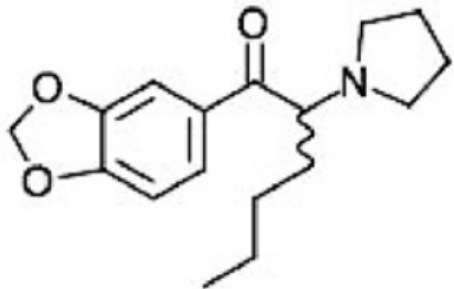
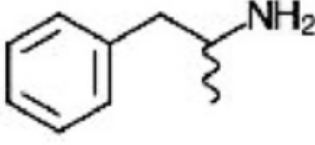
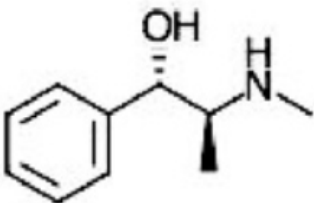
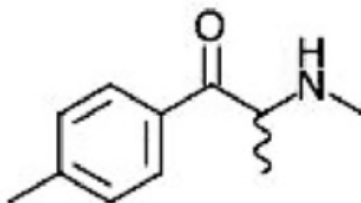
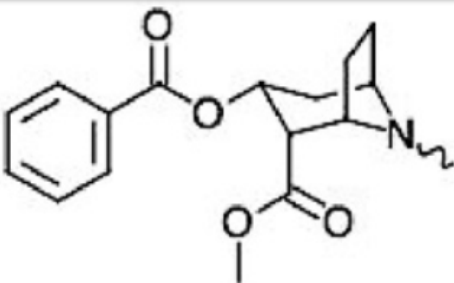


Cocaine/crack

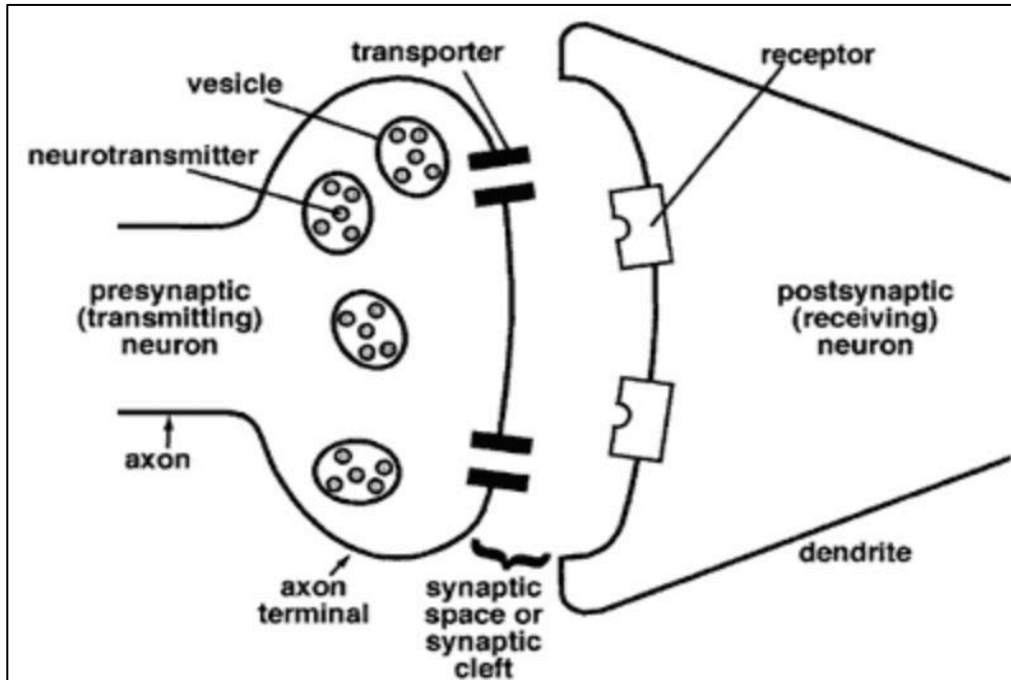
Amphetamine/methamphetamine



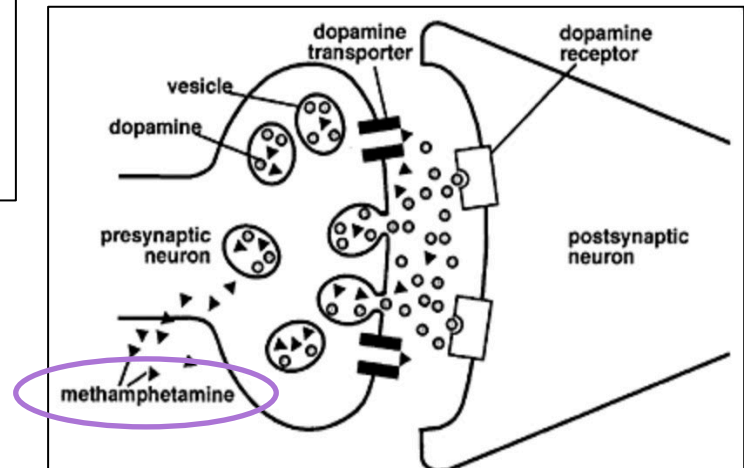
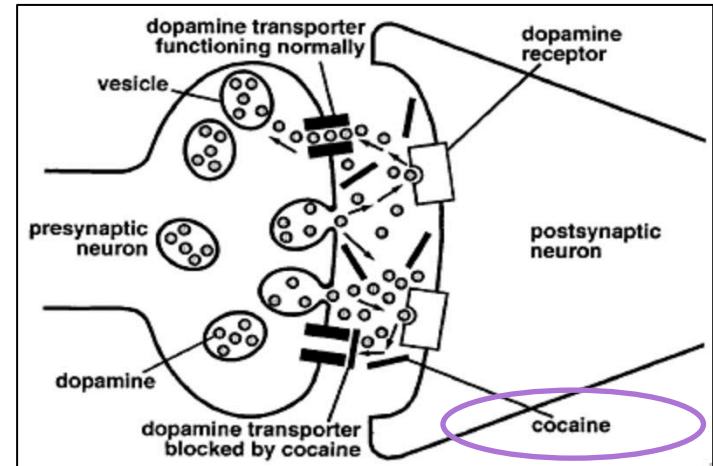
Background

| | | | |
|---|---|--|--|
|  |  |  |  |
| Methamphetamine | Ephedrine | MDMA | MDPV |
|  |  |  |  |
| Amphetamine | Pseudoephedrine | Mephedrone | Cocaine |
| All of the above compounds belong to the phenethylamine class of psychostimulants except cocaine; MDMA = methylenedioxymethamphetamine; MDPV = methylenedioxypropylvalerone | | | |

Background

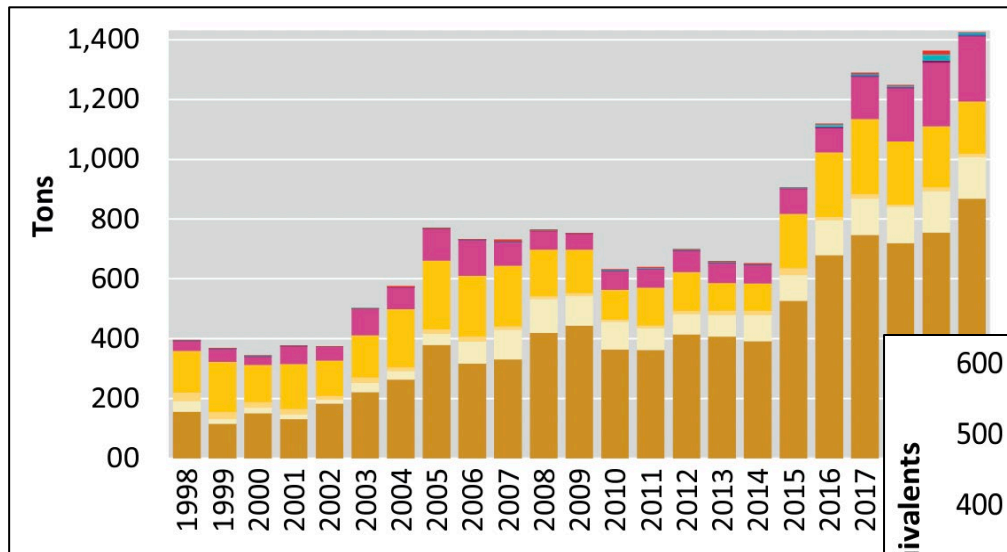


Increased monoamines = wakefulness, energy, sense of well-being, euphoria, excess sympathetic tone

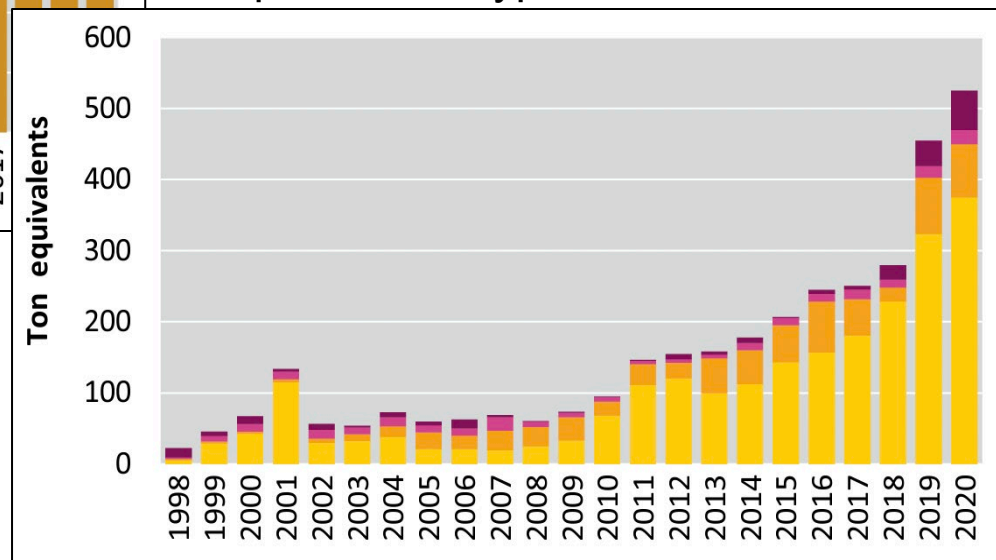


Epidemiology

Cocaine seizures

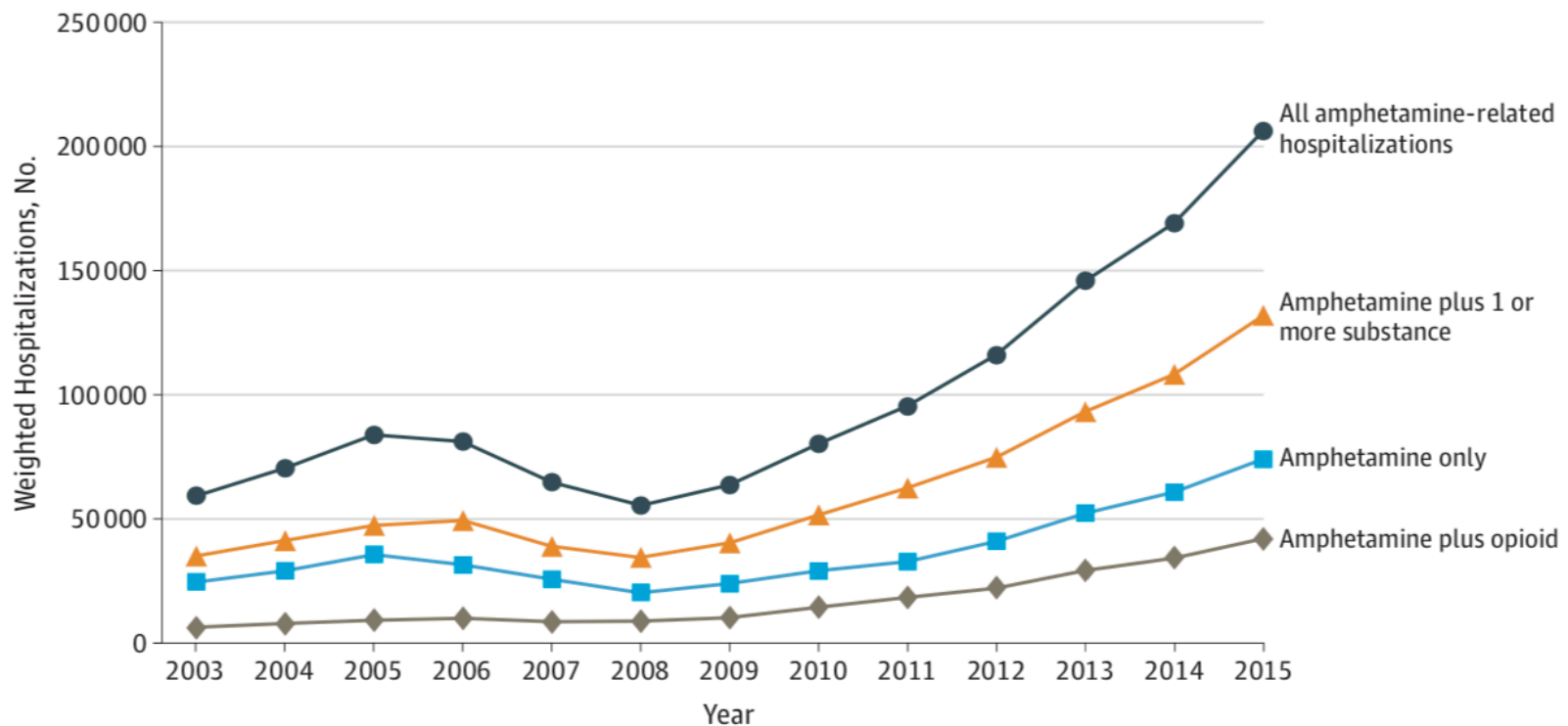


Amphetamine-type stimulant seizures



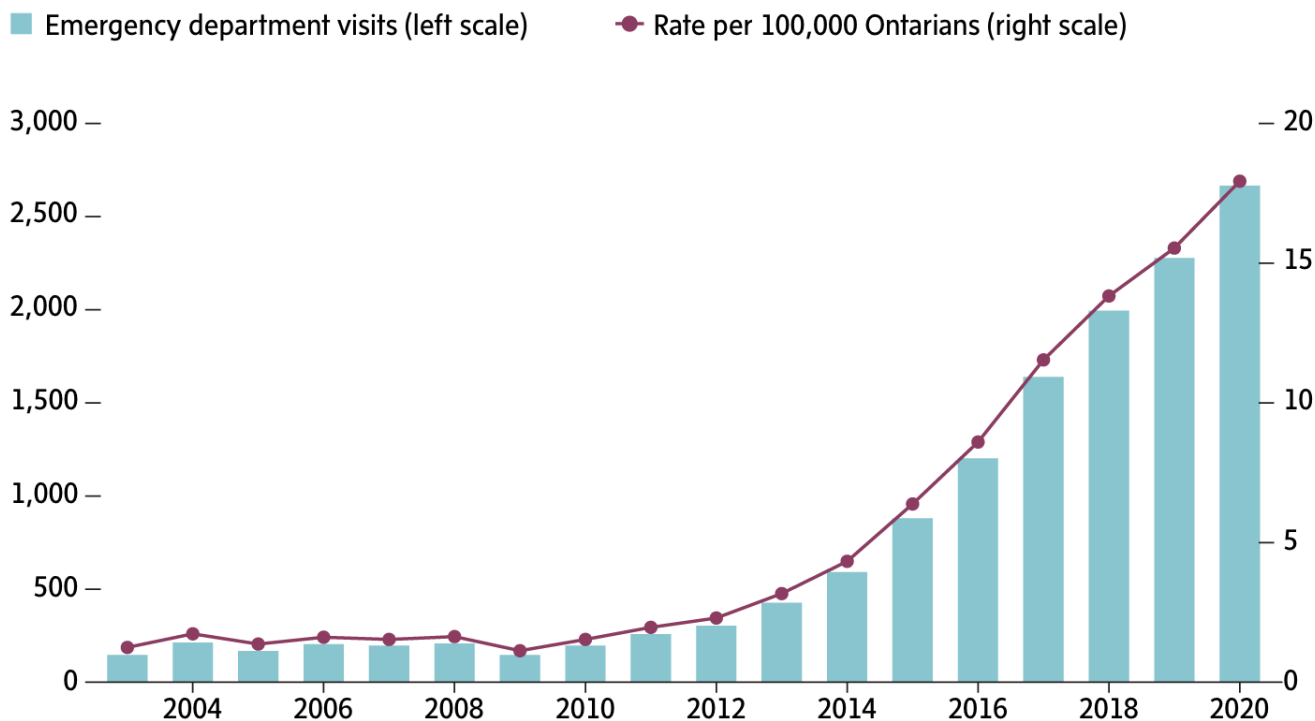
Epidemiology

Figure 1. Amphetamine-Related Hospitalizations in the United States, 2003 to 2015



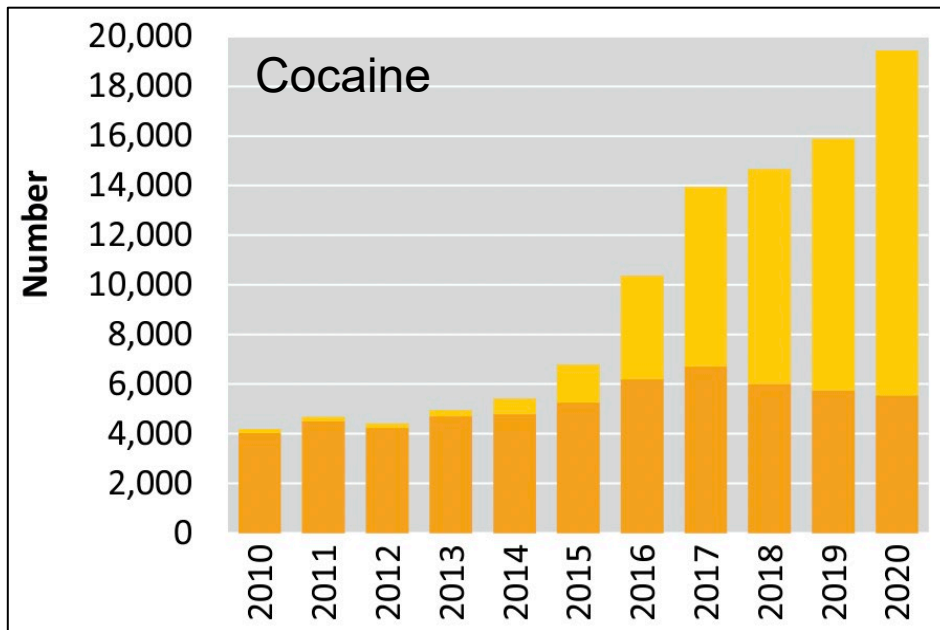
Epidemiology

Amphetamine-related emergency department visits in Ontario

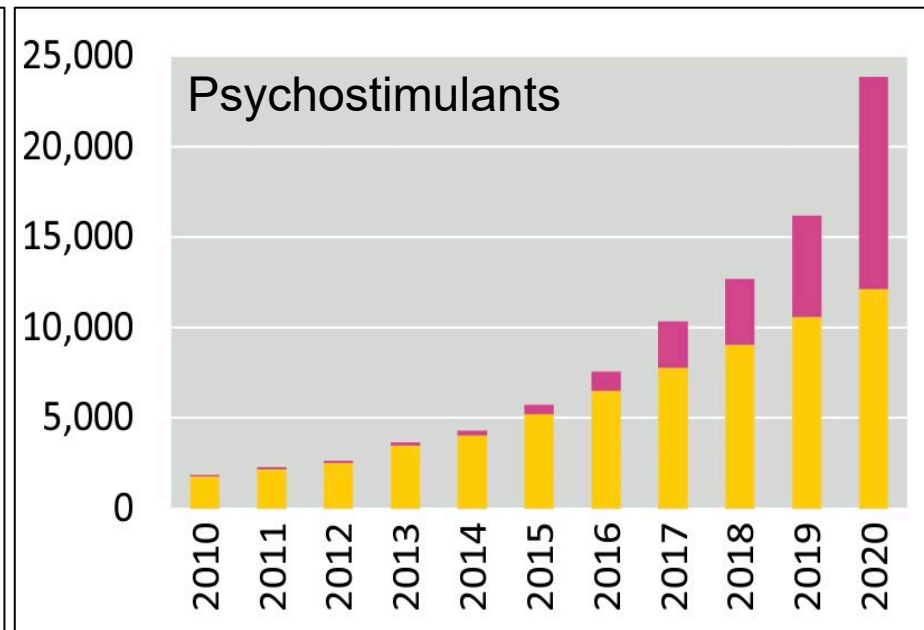


THE GLOBE AND MAIL, SOURCE: CRISPO JAG, LIU L, BACH P, ANSELL DR, SIVAPATHASUNDARAM B, NGUYEN F, KURDYAK P, SEITZ DP, CONLON M, CRAGG JJ. AMPHETAMINE-RELATED EMERGENCY DEPARTMENT VISITS IN ONTARIO, CANADA, 2003-2020. THE CANADIAN JOURNAL OF PSYCHIATRY

Overdose Deaths in the US



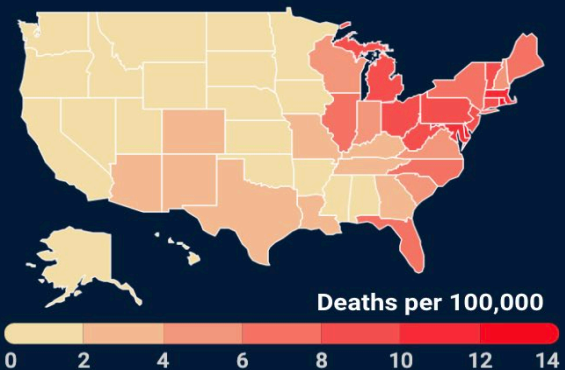
- Overdose deaths involving cocaine and synthetic opioids
- Overdose deaths involving cocaine without synthetic opioids



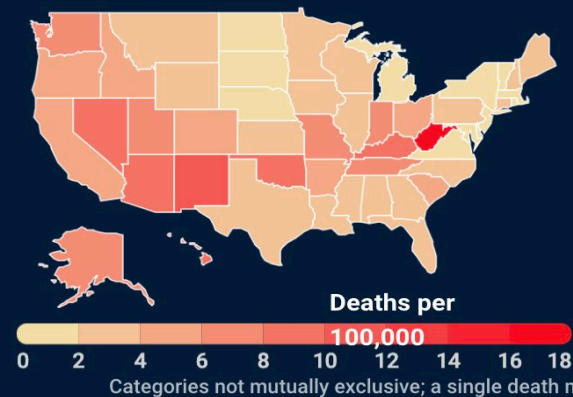
- Deaths involving psychostimulants and synthetic opioids
- Deaths involving psychostimulants without synthetic opioids

Overdose Deaths in the US

Different geographic patterns in death rates by stimulant type



Cocaine Deaths



Methamphetamine Deaths

- Patterns of use are highly regional, and may differ significantly among different populations
- Treatment approaches must be adapted to local resources, needs, drivers, patterns of use, etc.

Acute Intoxication

Symptoms

Mania/paranoia/psychosis

Hypertension, agitation, sweating

Skin-picking/formication (delusions of insects under the skin)

Abnormal movement
(choreoathetosis, ataxia)

Miosis

Management

Minimize stimulation:

- Quiet location
- Dimly lit
- Cool compress
- Soft voices

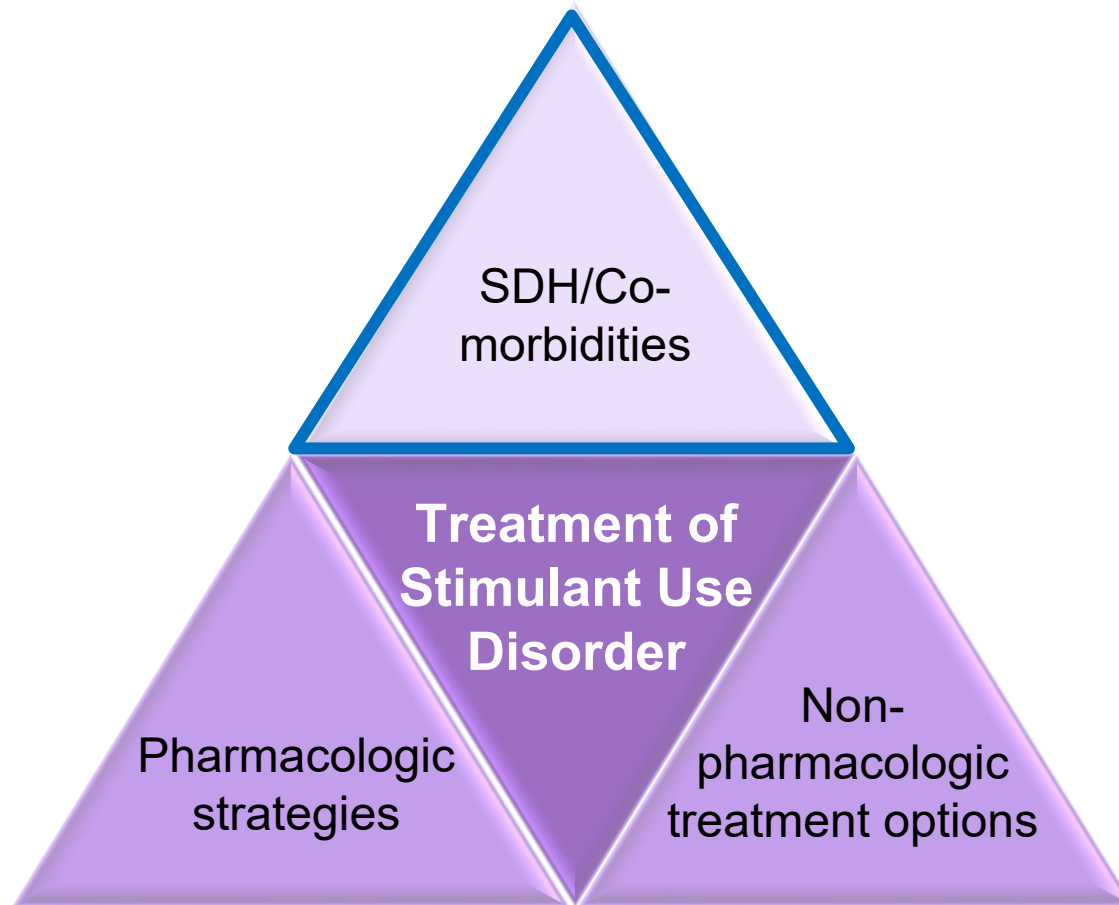
Food, water, blankets

Chemical sedation ONLY IF
ABSOLUTELY REQUIRED

- Benzos are first line

**How can we distinguish agitation/intoxication from frank psychosis?
How does this change management?*

Treatment



Psychosocial Treatment

1. Contingency management (CM)
2. Cognitive behavioural therapy (CBT)
3. Community reinforcement approach (CRA)
4. 12-step programs
5. Motivational interviewing
6. Meditation-based therapy
7. Non-contingent rewards
8. Psychodynamic therapy
9. Combinations programs
10. Bed-based treatment programs

Psychosocial Treatment

1. **Contingency management (CM)**
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Contingency Management

- Uses principles of operant conditioning to reduce reinforcement provided by drug use while simultaneously increasing reinforcement for healthier activities
- Applies contingencies in the form of positive rewards in order to promote goals such as reduction in substance use or retention in care
 - Voucher or cash based
 - Escalating rewards or “fish-bowl”
- In a meta-analysis of 50 RCTs effects of contingency management on abstinence at the end of treatment NNT = 5.44

Limitations: questionable long-term benefits, limited uptake due to moral objections

Cognitive Behavioural Therapy

- Short-term approach to help identify the thoughts, feelings, and actions that occur both before and after stimulant use
- Goal is to unlearn established habits and behaviours associated with use and learn more functional coping skills
- Helps patients to recognize situations in which they are likely to use drugs and to use coping skills to change their behaviour
- In a meta-analysis of 50 RCTs effects of CBT on abstinence at the end of treatment non-significant
- Individual studies have shown some benefit

Limitations: inconsistent results in the literature, requires specialist training

Community Reinforcement Approach

- Multicomponent approach that considers how environment influences habitual substance use
- Interventions include functional analysis, coping-skills training, and social, familial, recreational, and vocational reinforcements
- Focused on skills training, improving relations, employment and vocational counselling, and cultivating new activities and social networks
- In a meta-analysis of 50 RCTs effects of CM + CRA were strongest with NNT = 4.07 at end of treatment, NNT = 3.68 at longest follow-up

Limitations: complex and multi-layered, resource intensive, requires specific training

Choosing an Intervention

No guidance as to which intervention should be considered first

Include a **physical and psychosocial** assessment to help inform options

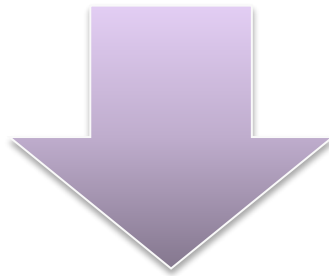
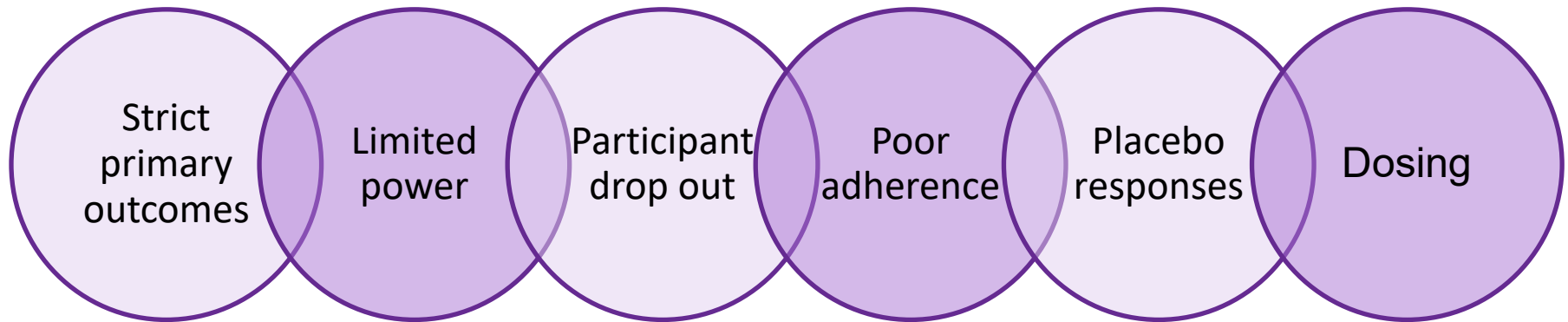
Discuss treatment options and rationale, including weighing of **risks and benefits**

Follow a **person-centred** and evidence-informed approach

Should be informed by the **individual's treatment goals and preferences**



Evidence for Pharmacotherapy



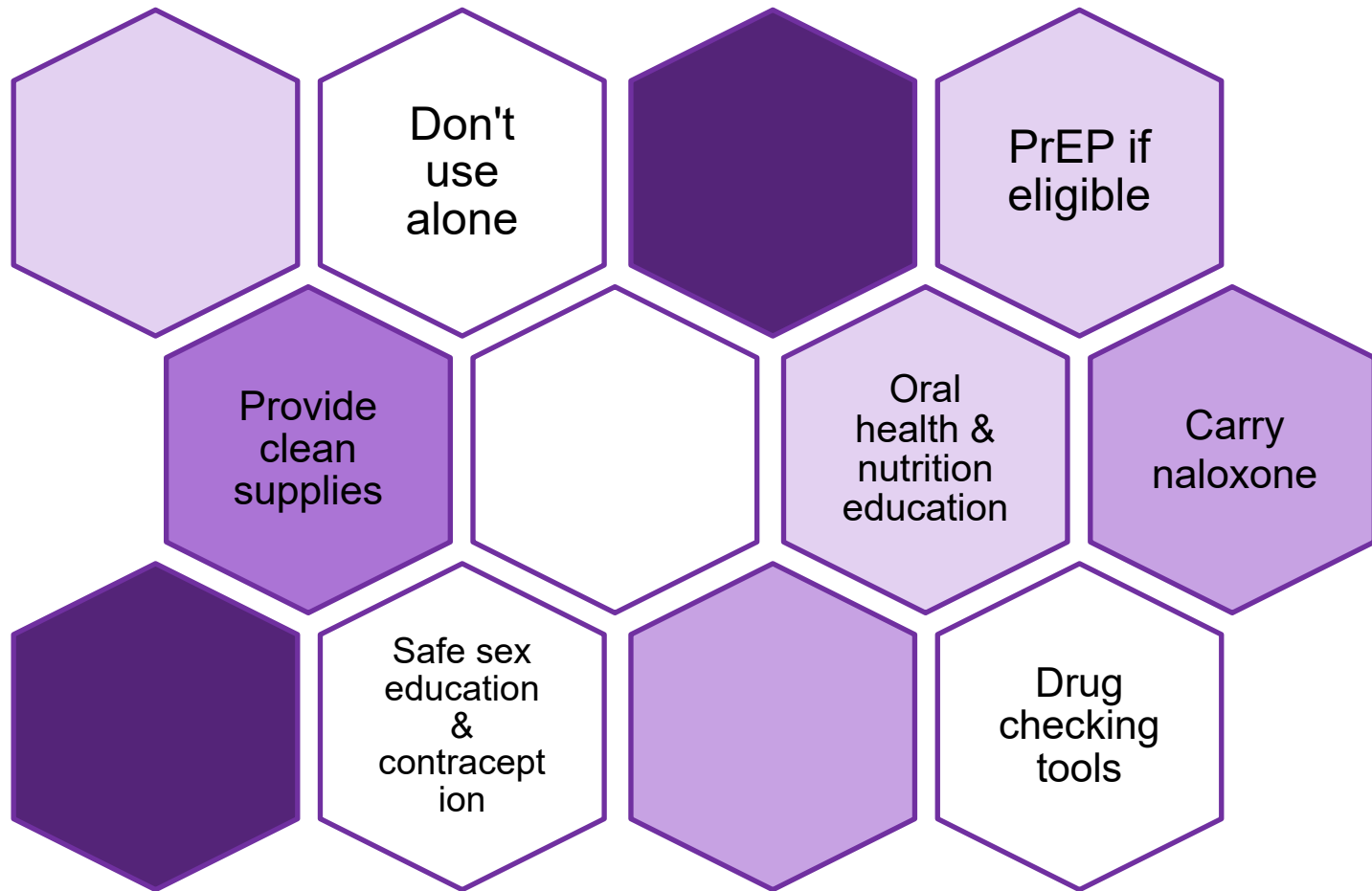
Conclusions are limited

Pharmacotherapy*

| Cocaine Use | Amphetamine Use |
|--|--|
| Bupropion | Mirtazapine |
| Modafinil <ul style="list-style-type: none">Without co-occurring alcohol use disorder | Bupropion (+/- Naltrexone-XR) <ul style="list-style-type: none">Monotherapy for low to moderate use onlyCombination therapy for those with alcohol use disorder |
| Topiramate (+/- Mixed Amphetamine Salts) <ul style="list-style-type: none">Consider with co-occurring alcohol use disorder | Topiramate <ul style="list-style-type: none">Consider with co-occurring alcohol use disorder |
| Amphetamine formulations <ul style="list-style-type: none">At or above highest recommended dose | Methylphenidate <ul style="list-style-type: none">At or above highest recommended dose |

**From DRAFT ASAM/AAAP guidelines for public comment*

Harm Reduction Principles



Additional Tips

- Stimulant withdrawal can be prolonged and miserable, don't minimize it
- Stimulants can be contaminated with fentanyl, counsel people accordingly on minimizing their overdose risk
- Beta-blockers **should not** be avoided in people who use stimulants when medically indicated

Start by trying to understand the role that a stimulant plays in someone's life and your treatment options will often become much clearer

Summary

- Cocaine and crystal methamphetamine are the most commonly used unregulated stimulants in North America
- Both prevalence and consequences of stimulant use are increasing and are contributing to the overdose crisis (especially methamphetamine)
- Management of intoxication and withdrawal is generally with supportive care
- Psychosocial and pharmacologic treatment options for stimulant use disorder do exist, contingency management is the best evidenced tool
- Harm reduction counseling is a critical component of care

References

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CME Post-Test Question #1

1. Which of the following is NOT a commonly used stimulant-type substance?

- a) Cocaine
- b) Crystal methamphetamine
- c) Phencyclidine
- d) MDMA

Correct Answer Feedback: That's correct! Phencyclidine is classified as a dissociative anaesthetic, all other choices are classified as stimulants.

Incorrect Answer Feedback: That's incorrect. Phencyclidine is classified as a dissociative anaesthetic, all other choices are classified as stimulants.

Reference: Vearrier D et al. (2012). Methamphetamine: History, Pathophysiology, Adverse Health Effects, Current Trends, and Hazards Associated with the Clandestine Manufacture of Methamphetamine. Dis Mon, 58:38-89.

CME Post-Test Question #2

2. Stimulants effects are mediated by which neurotransmitters/receptors in the central nervous system?

- a) Mu-opioid receptors
- b) Dopamine receptors
- c) NMDA receptors
- d) GABA receptors

Correct Answer Feedback: That's correct! Stimulants exert their effects on monoamine neurotransmitters such as dopamine, norepinephrine, and serotonin.

Incorrect Answer Feedback: That's incorrect. Stimulants exert their effects on monoamine neurotransmitters such as dopamine, norepinephrine, and serotonin.

Reference: Vearrier D et al. (2012). Methamphetamine: History, Pathophysiology, Adverse Health Effects, Current Trends, and Hazards Associated with the Clandestine Manufacture of Methamphetamine. Dis Mon, 58:38-89.

CME Post-Test Question #3

3. What percentage of psychostimulant-related overdose deaths in the US did not involve a synthetic opioid in 2020?

- a) 10%
- b) 20%
- c) 50%
- d) 90%

Correct Answer Feedback: That's correct! Approximately 50% of psychostimulant-related deaths in the US in 2020 did not involve a synthetic opioid.

Incorrect Answer Feedback: That's incorrect. Approximately 50% of psychostimulant-related deaths in the US in 2020 did not involve a synthetic opioid.

Reference: UNODC, World Drug Report 2022 (United Nations publication, 2022).

CME Post-Test Question #4

4. Which of the following is the best evidenced psychosocial intervention for the treatment of stimulant use disorder?

- a) Contingency management
- b) 12-step program
- c) Bed-based treatment programs
- d) Cognitive behavioural therapy

Correct Answer Feedback: That's correct! Cognitive behavioural therapy is the best evidenced treatment for stimulant disorder, especially when combined with a community reinforcement approach.

Incorrect Answer Feedback: That's incorrect. Cognitive behavioural therapy is the best evidenced treatment for stimulant disorder.

Reference: De Crescenzo F et al. (2018). Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis. PLoS Med, 15(12):e1002715.

CME Post-Test Question #5

5. Which of these medications has some evidence suggesting effectiveness in the treatment of stimulant use disorders?

- a) Dextroamphetamine
- b) Ranitidine
- c) Cyclobenzaprine
- d) Buprenorphine

Correct Answer Feedback: That's correct! Prescribed psychostimulants such as dextroamphetamine have some evidence supporting their role in the treatment of stimulant use disorders, especially cocaine use disorder.

Incorrect Answer Feedback: That's incorrect. Prescribed psychostimulants such as dextroamphetamine have some evidence supporting their role in the treatment of stimulant use disorders, the other medications do not.

Reference: Tardelli V et al. (2020). Prescription psychostimulants for the treatment of stimulant use disorder: a systematic review and meta-analysis. *Psychopharmacology*, 237(8):2233-2255.

CME Post-Test Question #6

6. Which of the following is NOT a recommended harm reduction intervention for people who use stimulants.

- a) Sterile injection equipment
- b) Naloxone kits/nasal spray
- c) Fentanyl test strips
- d) Lubricated eye drops

Correct Answer Feedback: That's correct! Sterile injection equipment, fentanyl test strips, and naloxone can all be helpful harm reductions for people who use stimulants.

Incorrect Answer Feedback: That's incorrect. Sterile injection equipment, fentanyl test strips, and naloxone can all be helpful harm reductions for people who use stimulants.

Reference: Bach P et al. (2022). British Columbia Centre on Substance Use Stimulant Use Disorder Practice Update. BCCSU, Vancouver, BC, Canada.